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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,825	02/25/2002	Man Sung Co	011823-004012US	5851

7590 04/23/2004

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EXAMINER	
HELMS, LARRY RONALD	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,825	CO ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claim 30 has been amended.

2. Claims 30-45 are pending and under examination.

3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

Specification

4. The disclosure is objected to because of the following informalities:

The amendment filed 2/24/04 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The first line of the specification has been updated to add the continuation data with a statement of incorporation by reference. Applicants are directed to the OG Notice:

United States Patent and Trademark Office OG Notices:
1268 OG 89 (18 March 2003).

Last paragraph of OG notice reads:

Part VII: Adding an Incorporation-By-Reference Statement in a Benefit Claim is Not Permitted After Filing. An incorporation-by-reference statement added after the filing

date of an application is not permitted because no new matter can be added to an application after its filing date. See 35 U.S.C. 132(a). If an incorporation-by-reference statement is included in an amendment to the specification to add a benefit claim after the filing date of the application, the amendment would not be proper. When a benefit claim is submitted after the filing of an application, the reference to the prior application cannot include an incorporation-by-reference statement of the prior application. See Dart Industries v. Banner, 636 F.2d 684, 207 USPQ 273 (C.A.D.C. 1980). Therefore, the Office will not grant a petition to accept a benefit claim that includes an incorporation-by-reference statement of a prior application, unless the incorporation-by-reference statement was submitted on filing of the application.

Inquiries regarding this notice should be directed to Eugenia A. Jones or Joni Y. Chang, Legal Advisors, Office of Patent Legal Administration, by telephone at (703) 305-1622.

February 24, 2003 STEPHEN G. KUNIN Deputy Commissioner for Patent Examination Policy

Applicant is required to cancel the new matter in the reply to this Office Action.

Rejections Withdrawn

5. The rejection of claims 30-45 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,350,861 is withdrawn in view of the filing of the terminal disclaimer.

6. The rejection of claims 30-45 under 35 U.S.C. 102(a) as being anticipated by Co et al (J. Immunology 148:1149-1154, 2/92) is withdrawn in view of the filing of the 132 Katz type declaration that was filed in the parent application.

Response to Arguments

7. The rejection of Claims 36-37 under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description is maintained.

The response filed 12/24/03 has been carefully considured but is deemed not to be persuasive. The response states that the hybridoma that produces the antibody was deposited under the Budapest treaty and cites US Patent 5,730,982, col. 5, lines 41-48. In response to this argument, it is still unclear if all of the assurances have been met. Further, there is no assurance that the depository would allow unlimited access to the material if the application has matured into a patent. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. In the absence of evidence that the hybridomas that produce the antibodies are readily available to the public and that all restrictions imposed by the depositor on the availiability to the public of the

deposited material will be irrevocably removed upon granting of a patent, applicant's arguments are not persuasive and the rejection is maintained.

8. Claims 30-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mutant antibody that comprises an amino acid substitution that eliminates a variable region framework glycosylation site of the parent wherein said elimination has the effect of increasing the affinity of the mutant relative to the parent, does not reasonably provide enablement for a mutant antibody that comprises an amino acid substitution that eliminates a variable region CDR glycosylation site of the parent wherein said elimination has the effect of increasing the affinity of the mutant relative to the parent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims is maintained.

The response filed 12/24/03 has been carefully considured but is deemed not to be persuasive. The response states that the Rudikoff reference does not support the Examiner's contentions in regards to glycosylation sites within the CDR and Rudikoff does not teach alteration of glycosylation sites within the CDR region and Rudikoff does not teach that all amino acid changes within a CDR will result in binding affiniy changes (see page 10-11 of response). The response further states that the specification does not teach mutations within the entire variable region of the immunoglobulin rather the mutations are limited to a small fraction of the amino acids within the variable region only where glycosylation sites are found and therefore identifying which sites to mutate

does not involve undue experimentation (see page 11 of response). In addition the response states that "Contrary to the Examiner's assertion, the specification teaches glycosylation through the entire variable region, not only within the framework region" (see page 10 of response). In response to this argument, Rudikoff illustrates the unpredictability in the art as far as alterations in the residues of a CDR and the affect on binding. While Rudikoff does state that substitutions in antibodies may result in altering antigen binding (as in a decrease in binding as illustrated in Rudikoff), Rudikoff does not indicate an increase in binding can be obtained by substitution as required in the claims. The response seems to contradict itself by saying that the specification teaches glycosylation through the "entire variable region" in one aspect and then states that the "mutations are limited to small fractions of the amino acids within the variable region". Although the specification does provide information as to how to identify which sites to mutate in the frameworks and in the CDRs, the specification does not demonstrate which residues to substitute or which residues when substituted would likely result in higher affinity as required in the claims. It would be undue experimentation to identify which residues to substitute in order to result in increased affinity. Just because one can identify the residues that need to be substituted does not result in producing an antibody that has an increase in affinity compared to the parent antibody. In addition, as stated the specification does not teach mutations within the entire variable region and in fact the specification only has one example of altering residue 73 in a framework region of a CD33 antibody and this one example resulted in an increase in affinity

compared to the parent. However, the claims encompass alterations in the entire variable region, including the CDRs.

The specification provides no direction or guidance regarding how to produce antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention.

Conclusion

9. No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 6:30 am to 4:00 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (571) 272-0871.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

571-272-0832